Hematopoietic and Lymphoid System Neoplasms

Survival Analysis

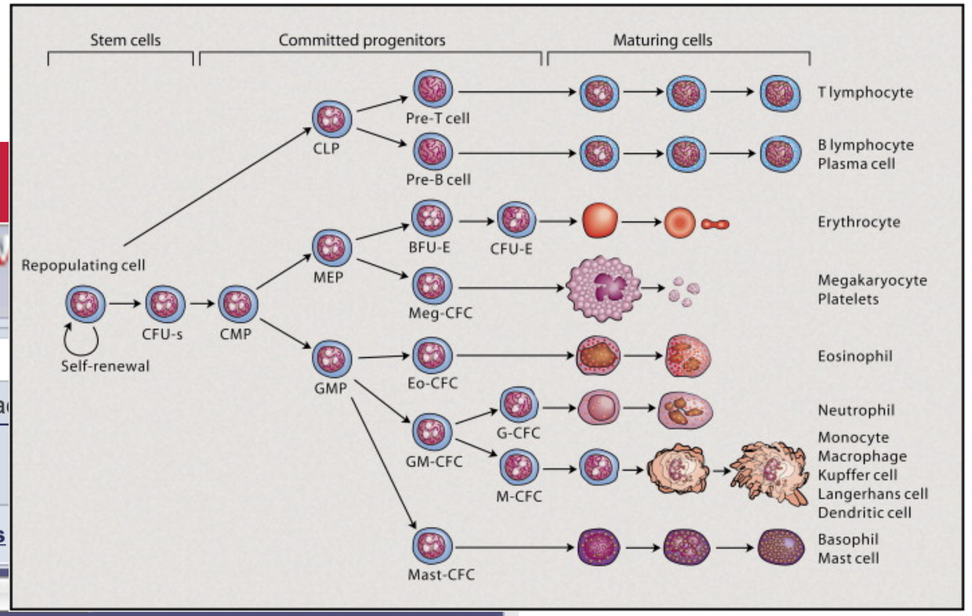
BIO392 - Bioinformatics of Sequence Variation

Kim and Sofia, 2022-10-07

Background

Background

Source: https://doi.org/10.1016/j.immuni.2007.05.012



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NCI Term Browser

Terminologies | Value Sets | Mappings

NCI thesaurus

Version:22.08e (Release date:2022-08-29)

C3720

Contains Exa

Name Code

Hierarchy | Value Sets

Quick Links

View in Hierarchy | View History | View Graph | Add to Cart | Suggest Changes

Hematopoietic and Lymphoid Cell Neoplasm (Code C27134)

Terms & Properties | Synonym Details | Relationships | Mappings | View All

Terms & Properties

Preferred Name: Hematopoietic and Lymphoid Cell Neoplasm

Definition: A neoplasm arising from hematopoietic cells found in the bone marrow, peripheral blood, lymph nodes and spleen (organs of the hematopoietic system). Hematopoietic cell neoplasms can also involve other anatomic sites (e.g. central nervous system, gastrointestinal tract), either by metastasis, direct tumor infiltration, or neoplastic transformation of extranodal lymphoid tissues. The commonest forms are the various types of leukemia, Hodgkin and non-Hodgkin lymphomas, myeloproliferative neoplasms, and myelodysplastic syndromes.

NCI-GLOSS Definition: A cancer of the blood or bone marrow, such as leukemia or lymphoma.

Background

	Incidence per 100’000 (USA)	5-Year Relative Survival
Leukemia	14.2	65.7%
Myeloma	7	57.9%
Non-Hodgkin Lymphoma	19.2	73.8%
Hodgkin Lymphoma	2.6	89.1%

Data sources:
https://seer.cancer.gov
https://cancerstatisticscenter.cancer.org

Survival Analysis on lymphoma.csv

- Study CNVs in samples with mutations in the following genes:
  - TP53-
  - CDKN2A-
  - ERBB2+
  - MYC+

Survival Analysis on lymphoma.csv

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  - **TP53- (Godley et al, 2017)**
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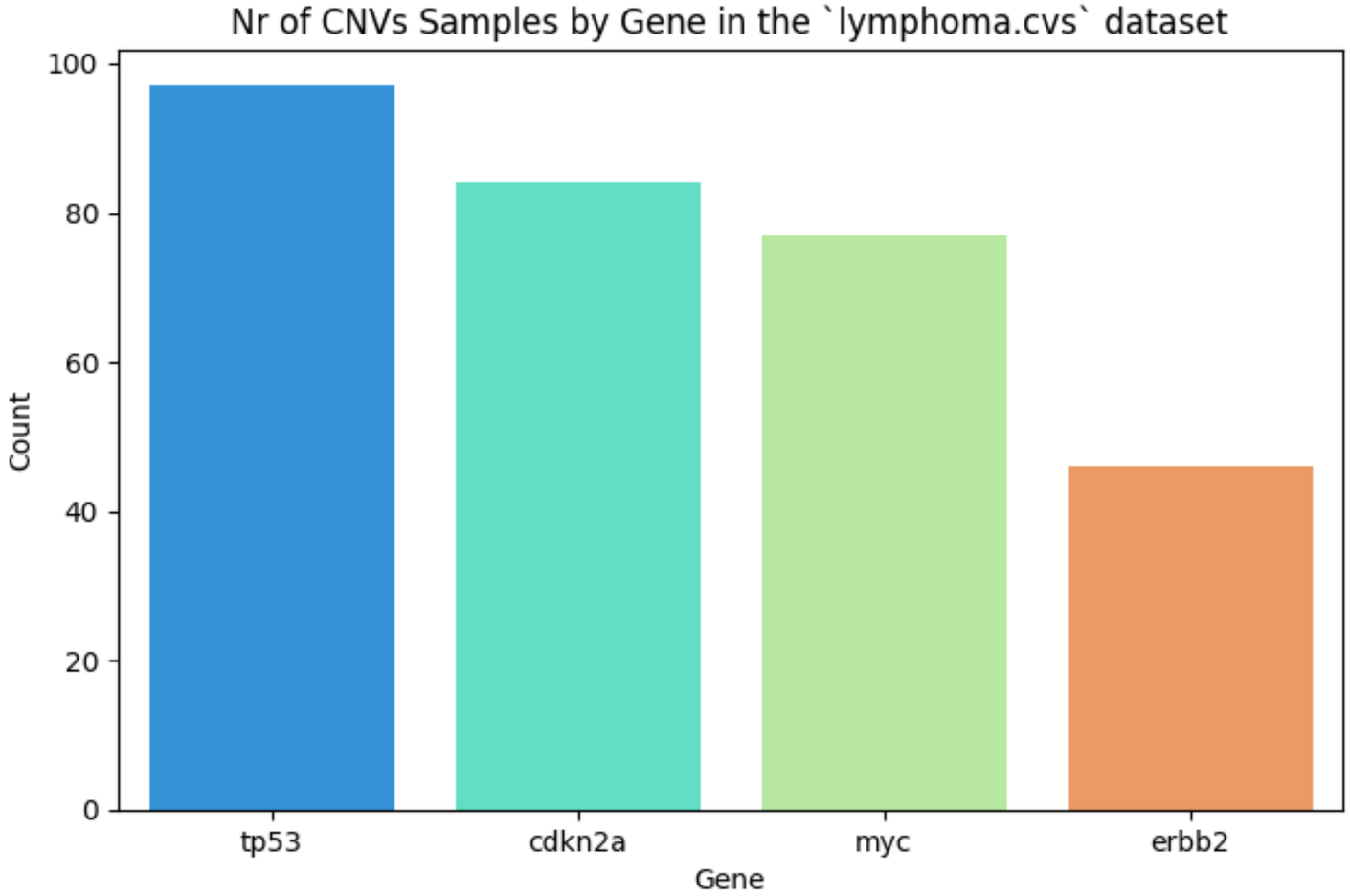
  - ERBB2+
  - **MYC+ (Skibola et al, 2010)**

Evidence of poor prognosis

in hematopoietic and lymphoid system malignancies

Dataset

lymphoma.csv



After matching…

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Int64Index[illegible] 237 entries, [illegible]4 to 48
Data columns (total 9 columns):
 #   Column                          Non-Null Count  Dtype
---  ------                          --------------  -----
 0   info.followupMonths             237 non-null    float64
 1   info.death                      237 non-null    int64
 2   group                           237 non-null    object
 3   histologicalDiagnosis.id        237 non-null    object
 4   info.cnvstatistics.cnvfraction  237 non-null    float64
 5   sex                             237 non-null    object
 6   pathologicalStage.label         237 non-null    object
 7   info.cnvstatistics.dupfraction  237 non-null    float64
 8   info.cnvstatistics.delfraction  237 non-null    float64
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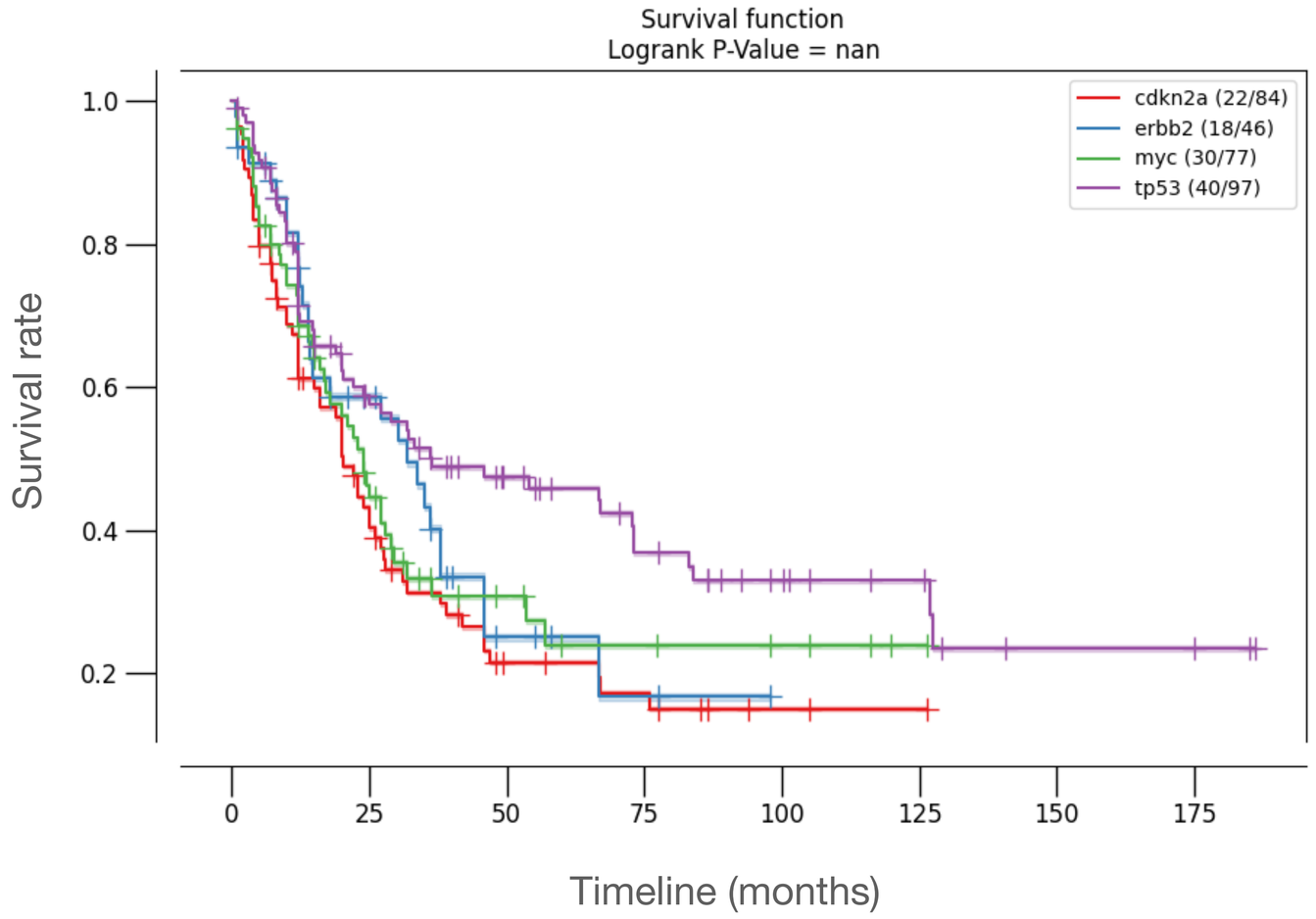
Results

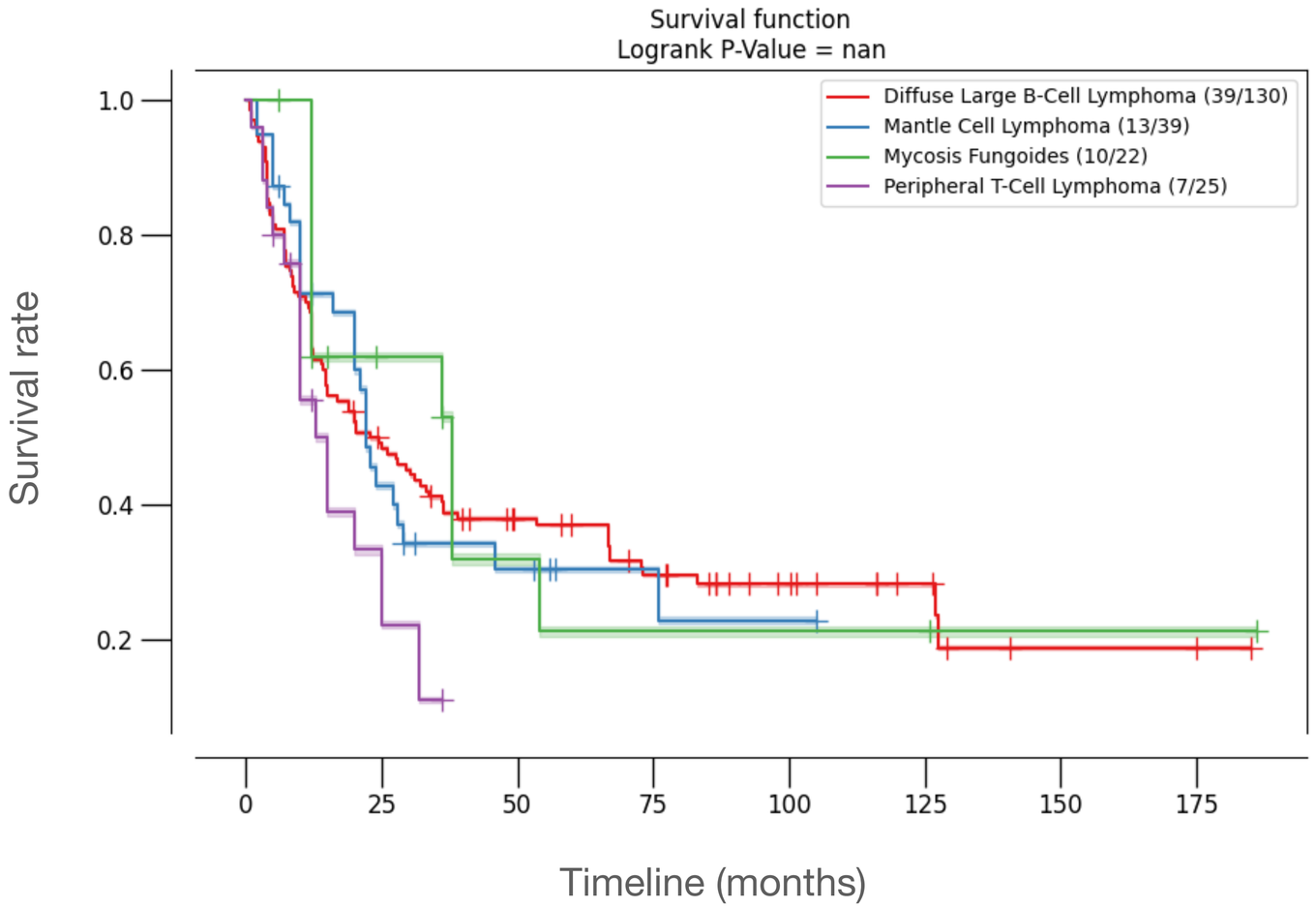
KM Curves

Survival rate based on gene



KM Curves

Survival rate based on tumor type

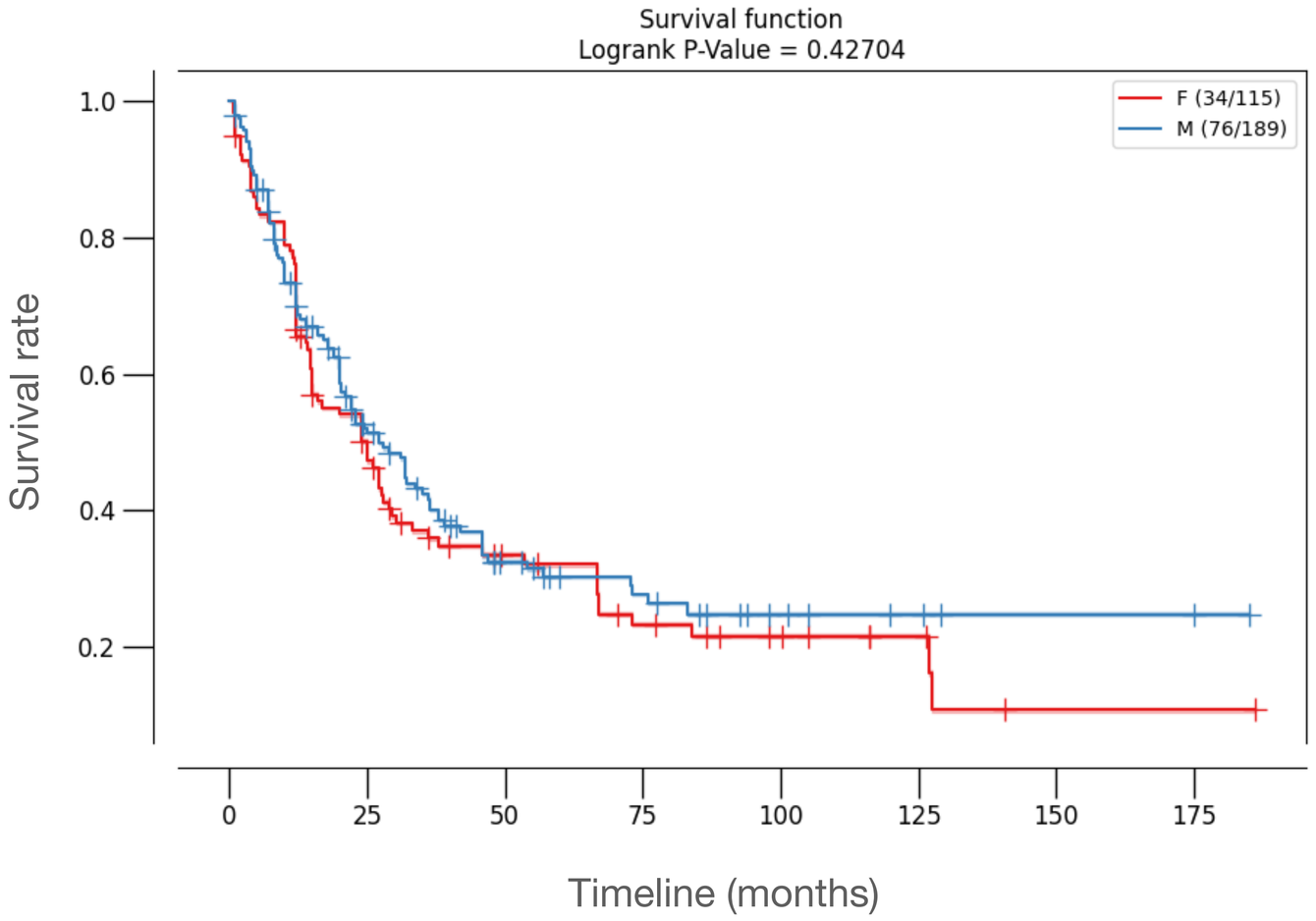


Note 1: plot excluded tumor types with sample size < 5

Note 2: Mycosis Fungoides is also T-cell Lymphoma

KM Curves

Survival rate based on sex of the patient



CNV fraction

Does CNV fraction change across samples with different mutated genes?

CNV fraction

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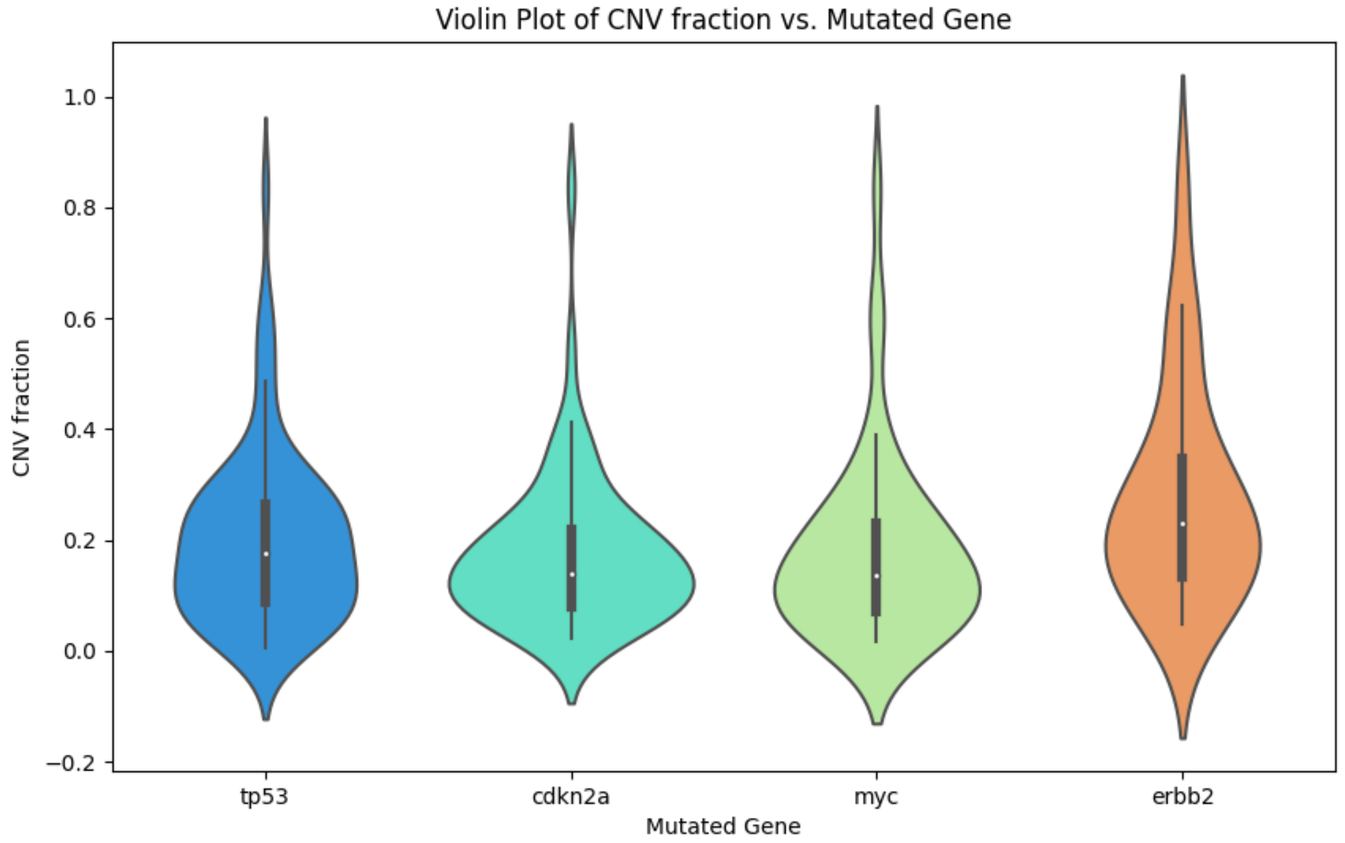

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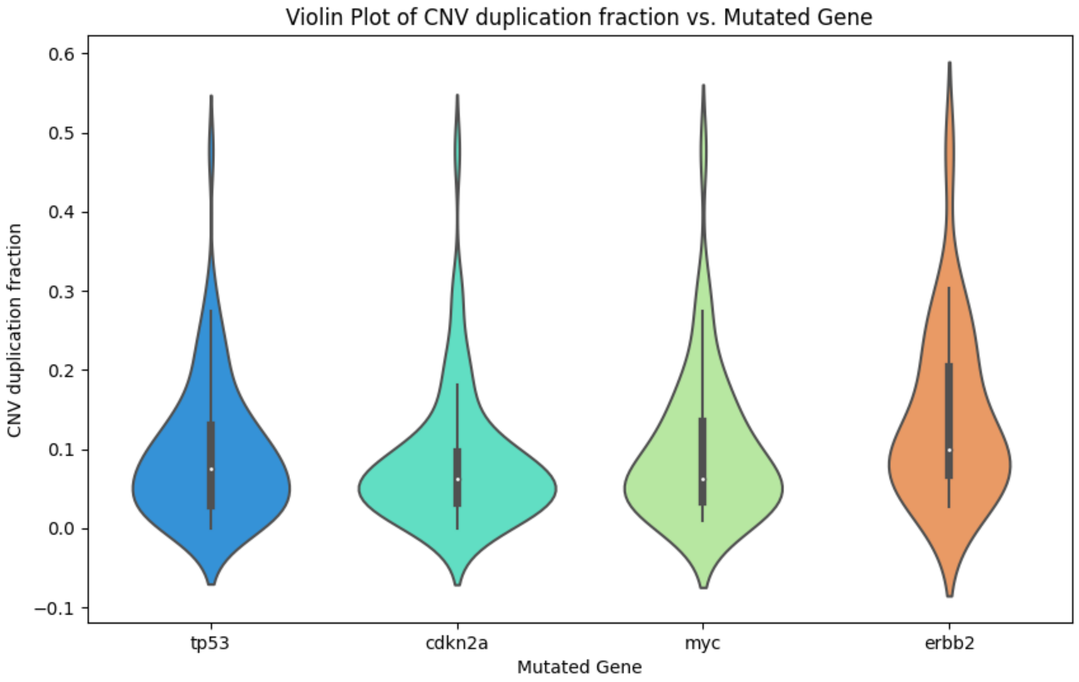

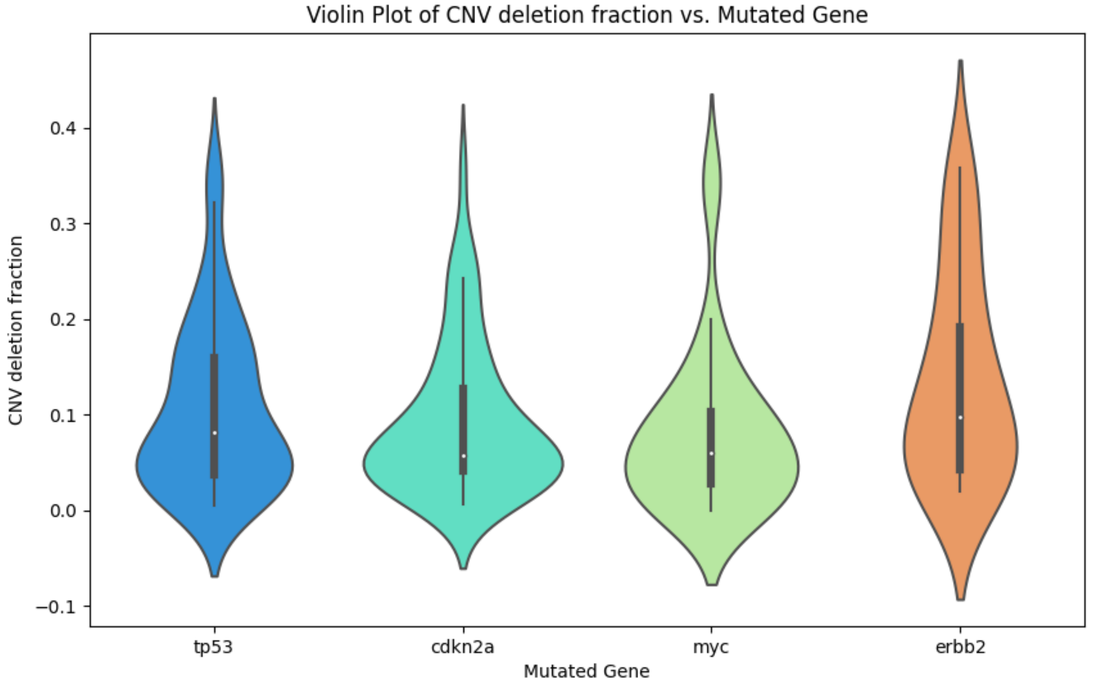

CNV fraction

Does CNV fraction change across tumor types?

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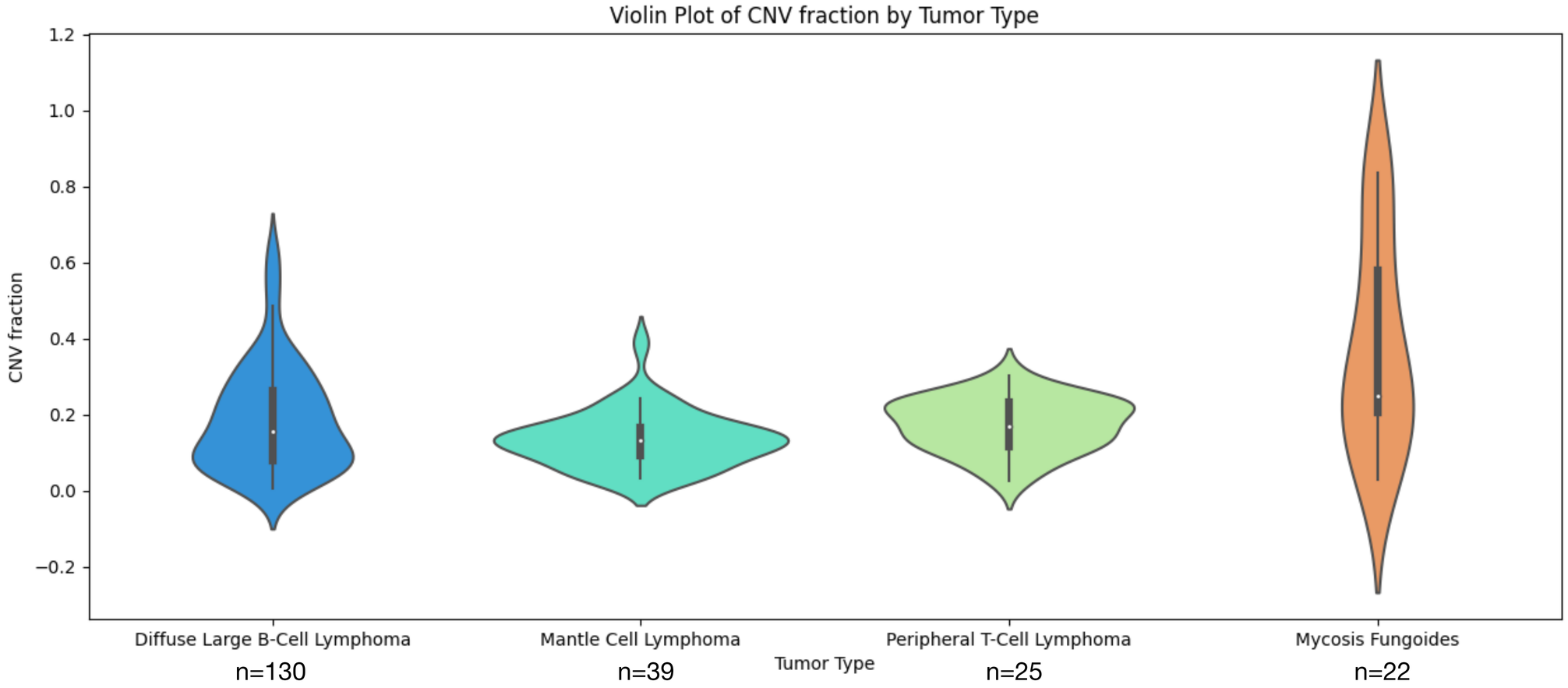

CNV fraction

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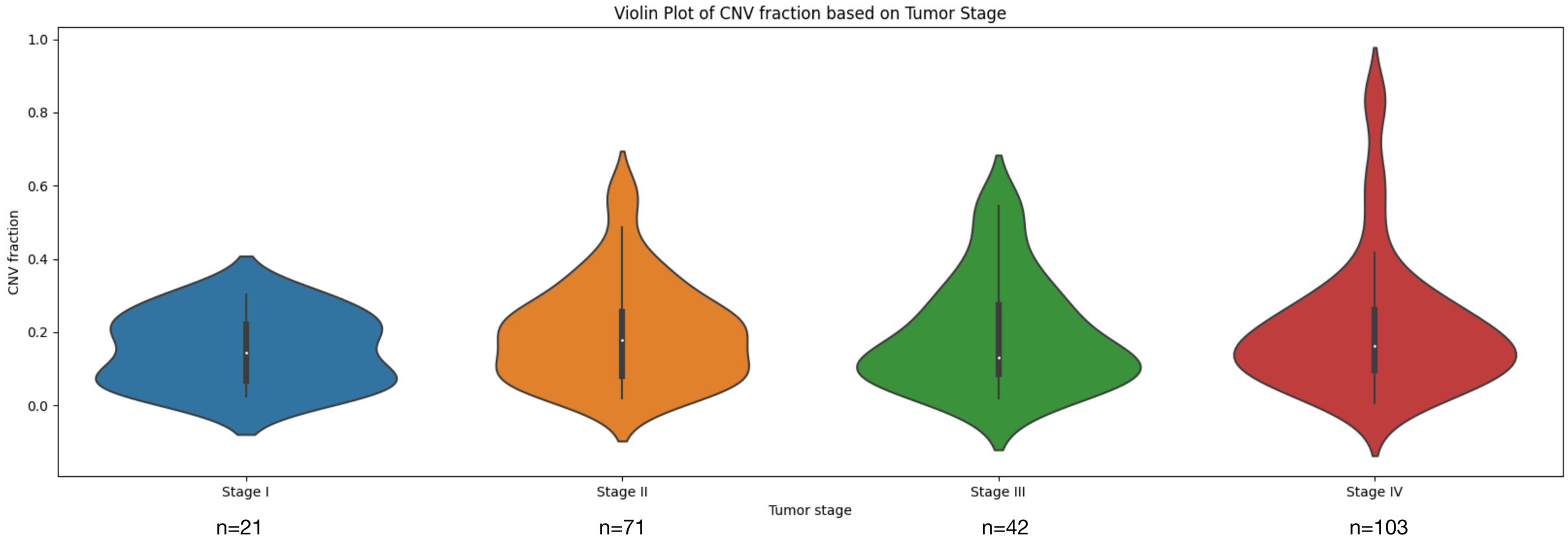

Summary

Summary I: survival rate

- (Significant) difference in survival rate depending on the mutated gene
  - ↑Higher survival rate in patients with TP53 mutations (unexpected - maybe due to small sample size)
- (Significant) difference in survival rate depending on the tumor type
  - Peripheral T-cell lymphoma patients have ↓lowest survival rate
- No significant difference in survival rate between male and female patients

Summary II: CNV fraction

- CNV fraction has **similar** distributions across the different mutated genes
  - Data indicates CNV fraction of the **whole** genome - not of the single mutated gene
- CNV fraction has **different** distributions depending on tumor types
- CNV fraction is **similar** at all tumor stages
  - Disease progression doesn’t seem to cause more CNVs (unexpected)

Comments and Outlook

1. No myeloma (and leukemia) tumor samples: expected ↓lower survival rate compared to lymphomas
2. Sample size:
    A. Increase the overall sample size to get more significant observations
    B. Ensure similar sample sizes when comparing groups
3. Get CNV data for oncogene or TSG sequence instead of working with whole genome CNV data: compare CNV fractions between the genes of interest

Thank you! :-)
Questions?

References

Articles

Godley, L. A., & Shimamura, A. (2017). Genetic predisposition to hematologic malignancies: management and surveillance. *Blood, The Journal of the American Society of Hematology*, *130*(4), 424-432.

Lopez-Santillan, M., Lopez-Lopez, E., Alvarez-Gonzalez, P., Martinez, G., Arzuaga-Mendez, J., Ruiz-Diaz, I., ... & Martin-Guerrero, I. (2021). Prognostic and therapeutic value of somatic mutations in diffuse large B-cell lymphoma: A systematic review. *Critical Reviews in Oncology/Hematology*, *165*, 103430

Skibola, C. F., Curry, J. D., & Nieters, A. (2007). Genetic susceptibility to lymphoma. *Haematologica*, *92*(7), 960.

Webpages

https://seer.cancer.gov
https://cancerstatisticscenter.cancer.org
https://ncit.nci.nih.gov/ncitbrowser/
https://progenetix.org